REMARKS

Claims 1-8 are pending. Claims 5-8 have been withdrawn from consideration by the Examiner as being directed to a non elected invention. Claims 1-4 and 8 are currently amended without prejudice to the canceled subject matter. Claims 9-14 are newly added. Support for these amendments can be found throughout the specification and claims as originally filed. No new matter has been entered.

Claims 1-4 have been amended so as to remove subject matter directed to DNA material comprising the xylA promoter. DNA material comprising the xylA promoter has been transferred to the set of newly added claims 9-11.

Withdrawn claim 8 has been amended to correct punctuation.

Newly added claim 12 recites DNA comprising a sequence selected from the group comprising (i) a sequence at least 95% identical to (SEQ ID NO:5); (ii) a sequence at least 98% identical to (SEQ ID NO:5) and (iii) a sequence at least 99% identical to (SEQ ID NO:5).

Newly added claim 13 recites DNA comprising a sequence selected from the group comprising (i) a sequence at least 95% identical to (SEQ ID NO:6); (ii) a sequence at least 98% identical to (SEQ ID NO:6) and (iii) a sequence at least 99% identical to (SEQ ID NO:6).

Newly added claim 14 further limits claim 11 by specifying that the reporter gene is luciferase.

Support for newly added claims 12, 13 and 14 is found throughout the specification, particularly page 8, lines 1-8.

Specification

The office action indicates that the title of the invention is not descriptive. Accordingly, Applicant has amended the title so that it is clearly indicative of the invention to which the claims are directed.

Claims Rejections- 35 U.S.C. § 101

Claims 1-4 are rejected under 35 USC 101 for being directed to nonstatutory subject matter. The office action indicates that the claimed products are not distinguished from natural products which are considered non statutory subject matter. Accordingly, the claims have been amended to indicate the hand of the inventor by the recitation of an *isolated* DNA.

Claims Rejections- 35 U.S.C. § 112, first paragraph

Claim 4 is rejected under 35 USC 112, first paragraph, because the office action states that the specification, while being enabled for an isolated DNA comprising the sequence of SEQ ID NO:5 or SEQ ID NO:6, does not reasonably provide enablement for any DNA material containing any sequence that is at least 90% identical to the sequence of SEQ ID NO:5 or SEQ ID NO:6.

Applicant respectfully traverses.

Claim 4 and newly added claim 9 are directed to nucleic acid constructs comprising SEQ ID NO:5 and SEQ ID NO:6, respectively. SEQ ID NO:5 and SEQ ID NO:6 encode a T7 promoter or the xylA promoter, respectively, a ribosome binding site from a Gram-positive bacterium, and a reporter gene, which is operably linked to the promoter.

As disclosed in the specification, SEQ ID NO:5 and SEQ ID NO:6 are components of two different reporter plasmids, referred to as pT7-FF and pXyl-FF,

respectively, which enables a non-radioactive *in vitro* coupled transcription/translation assay suitable for all important Gram-positive pathogens including Staphylococci, Pneumococci and Enterococci.

> " Two reporter plasmids, pT7-FF and pXyl-FF were constructed using S30 extracts from Gram-positive bacteria, for use in the in vitro coupled transcription/translation assay. Both plasmids contain the eukaryotic firefly luciferase gene as reporter gene enabling a bioluminescence read-out, which can be easily measured. Plasmid pT7-FF contains the bacteriophage T7 promoter and the SD sequence from the S. aureus capA1 promoter [2], whereas plasmid pXyl-FF contains the SD and promoter sequences of the S. xylosus xylA promoter [3] (FIG. 1). Both plasmids, pT7-FF and pXyl-FF, can be easily propagated in E. coli. The xylA promoter was chosen because of its strong expression in staphylococci [3]. The T7 promoter is also known as a strongly transcribed promoter and an in vitro coupled transcription/translation assay using S30 extracts from E. coli supplemented with T7 RNA polymerase is commercially available from Promega Corporation. Moreover, a radioactive in vitro transcription/translation assay driven by the T7 promoter was described for S. carnosus [4]". emphasis added,[0014] of the published application

In view of the description above, Applicant respectfully disagrees with the office action's asserts that the specification does not provide guidance prediction and working examples showing a correlation between any structure, nucleotide composition and nucleotide sequence of the nucleic acid molecules as claimed and its biological function. Applicant contends it would be well with in the ability of one of skill in the art at the time of the invention to make and use the genus of nucleic acids having at least 90% identity with SEQ ID NO:5 and SEQ ID NO:6, in transcription/translation assays as disclosed using the explicit guidance disclosed in the instant specification, particularly in its working examples.

Thus, Applicant disagrees with the contention in the office action that the amount of experimentation necessary is undue. As noted, "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re*

Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine.'" *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Given the well established components of the claimed sequences and the explicit working examples detailing the construction and use of their use in a transcription/translation assays, Applicant contends that no more than mere routine experimentation would be required in the hands of a person skilled in the art to practice the full scope of the claimed invention.

Claims Rejections- 35 U.S.C. § 102

Claims 1 and 3 are rejected under 102(b) as being anticipated by Bhavsar *et al.*

> Anticipation requires that the purported prior art reference disclose each and every limitation of the claim. *Atlas Powder Company et al. v. IRECO, Incorporated et al.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999).

The office action indicates that Bhavsar *et al.* teaches a plasmid (pSWEET) containing the ribosomal binding site from *B. subtilis* and the xylA promoter operably linked to a reporter gene encoding beta galactosidase.

Applicant respectfully traverses on the grounds that the cited art does not teach all the limitations of the claims as newly amended. Specifically, the claimed limitation that the recited DNA comprise a T7 promoter and a ribosome binding site from a Gram-positive bacterium, and a reporter gene, which is operably linked to the promoter, is not taught by Bhavsar *et al.* Because the cited reference does not teach all the limitations of the instant claims as newly amended, it does not destroy the novelty of the claims.

In view of the claim amendments and remarks, Applicant respectfully requests reconsideration and withdrawal of the instant rejection.

Claims Rejections- 35 U.S.C. § 103(a)

Claim 2 is rejected as being unpatentable over Bhavsar *et al.* in view of Kain *et al.*

Applicant respectively traverses.

Graham v. John Deere Co., 338 U.S. 1, 148 USPQ 459 (1966), recently reaffirmed by *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 USPQ2d 1385 (2007), provides the analytical framework for determining obviousness. Under *Graham*, obviousness is a question of law based on underlying factual inquires that address (1) the scope and content of the prior art, (2) the differences between the claimed invention and the prior art, and (3) the level of ordinary skill in the pertinent art. Evidence of secondary factors (e.g., commercial success, long-felt but unmet need, and unexpected results) are also given weight in the analysis. Moreover, to establish a prima facie obviousness rejection of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Predictability is required in maintaining a legal conclusion of obviousness under both KSR and the USPTO published guidelines.

The office action asserts it would have been obvious to one of ordinary skill at the time the invention was made to have modified the pSWEET plasmid taught by Bhavsar *et al.*, by replacing its beta galactosidase reporter gene with the luciferase reporter gene taught by Kain *et al.* , because luciferase is a widely used reporter enzyme which is much faster and more sensitive then the CAT assay and does not use radioactivity.

The plasmid (pSWEET) taught by Bhavsar *et al.* contains the ribosomal binding site from *B. subtilis* and the xylA promoter operably linked to a reporter gene encoding beta galactosidase.

Applicant respectfully traverses on the grounds that the cited references, either individually or when combined, do not arrive at the instant invention with all the limitations of the claims as newly amended. As newly amended, claim 1 recites an isolated DNA material comprising a T7 promoter, a ribosome binding site from a Gram-positive bacterium, and a reporter gene, which is operably linked to the promoter. Thus, the instantly rejected claim 2, which depends from claim 1, no longer recites DNA material which comprises a xylA promoter.

Since the pSWEEET plasmid taught by Bhavsar et al. contains a xyla promoter, and not the T7 promoter as required by the instant claims, and since the teachings of Kain et al. do not make up for Bhavsar et al.'s lack of teaching of the T7 promoter, the cited references, either individually or in combination, do not arrive at the claimed invention with all its recited limitations. Thus according to *In re Royka*, a prima facie case of obviousness over claim 2, as newly amended, has not been established.

Withdrawal and reconsideration of the rejection of instant claim 2, as newly amended, is respectfully requested.

Applicant has newly added claim 9, which recites an isolated DNA material comprising the xylA promoter, a ribosome binding site from a Gram-positive bacterium, and a reporter gene, which is operably linked to the promoter, wherein the reporter gene is luciferase.

Applicant anticipates that the Examiner will apply the instant rejection to newly added claim 9, i.e., that it would have been obvious to have modified the pSWEET plasmid taught by Bhavsar *et al.*, by replacing its beta galactosidase reporter gene with the luciferase reporter gene taught by Kain *et al.* The Examiner's basis for this substitution would be that luciferase is a widely used reporter enzyme which is much faster and more sensitive then the CAT assay and does not use radioactivity. While not refuting Kain *et al.*'s characterization of the luciferase gene's speed and sensitivity as a reporter gene, Applicant contends that one of skill in the art at the time of the invention could not have

reliably predicted the functionality of the DNA material comprising the xylA promoter, a ribosome binding site from a Gram-positive bacterium, and a luciferase reporter gene operably linked to the promoter, as required recited in newly added claim 9.

As discussed above, predictability is required in maintaining a legal conclusion of obviousness under both KSR and the USPTO published guidelines. For instance, one guideline published by the USPTO for determining obviousness after KSR (Federal Register, Vol. 72, No. 195; October 10, 2007) is simple substitution of one known element for another to *obtain predictable results.* However, the office action provides no grounds on which one of skill could ascertain that combining the separate promoter (xylA) and reporter elements (luciferase) taught independently by Bhavsar *et al.* and by Kain *et al.*, respectively, could be operably linked as claimed. That is, one of skill could not reliably predict that replacing the beta galactosidase reporter gene of the pSWEET plasmid (containing the xylA promoter) with the luciferase reporter taught by Kain *et al.* would produce a stable functioning construct as claimed. Without evidence that one of skill in the art could have predictably arrive at the claimed invention based on the teachings of the cited references, a prima facie case of obviousness has not been achieved.

Further, Applicant respectfully submits that the combination of Bhavsar *et al.* and Kain *et al.* is the result of hindsight. There is no teaching or suggestion in Kain *et al.* that its teachings of the luciferase reporter gene should or could be used as a replacement for the beta galactosidase reporter gene in the constructs containing the xylA promoter taught by Bhavsar *et al.* or any other reference, to produce the claimed DNA material comprising the xylA promoter, a ribosome binding site from a Gram-positive bacterium, and a luciferase reporter gene operably linked to the promoter. Thus, it would not have been predictable based on the cited art to one of skill in the art at the time the invention was made, who was considering combining the methods of Bhavsar *et al.* and Kain *et al.* by substituting the luciferase reporter gene as the reporter gene in the constructs taught Bhavsar et al. to use in a transcription/translation assay, that such a combined method would be successful and/or would predictably arrive at the claimed invention. Thus, the cited references would only be

combined by one of skill having the benefit of Applicant's specification. Such a combination is hindsight which is not permissible.

Conclusion

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

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